

Aetiology of urinary symptoms in sexually active women

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SUMMARY Two hundred and fifty six unselected women, 50 of whom had urinary symptoms (frequency of urination or dysuria, or both), and who were attending a department of genitourinary medicine, were investigated. The urinary symptoms were associated both with pyuria and the isolation of undoubted pathogens from midstream urine (MSU) specimens. No associations were found between urinary symptoms and the isolation of *Neisseria gonorrhoeae* or *Chlamydia trachomatis* from the urethra or cervix; the recovery of *Mycoplasma hominis* from the urethra, cervix, or MSU; the recovery of *Trichomonas vaginalis* or *Candida albicans* from the vagina; or the presence of bacterial vaginosis. Urethral leucocytosis was associated with the isolation of *T. vaginalis* but not with the recovery of *N. gonorrhoeae*, *C. trachomatis*, *C. albicans*, or urinary pathogens. Pyuria was associated with the isolation of urinary pathogens and with the presence of trichomoniasis; it was not associated with the recovery of *C. trachomatis* or *M. hominis*.

Introduction

The presence of multiple pathogens makes the cause of frequent urination and dysuria in sexually active women difficult to ascertain. Episodes of dysuria, with or without frequent urination, are common in women. In about half, bacterial cystitis is diagnosed by confirming significant bacteriuria. This term, introduced by Kass,¹ is defined as a pure growth of $\geq 10^5$ organisms/ml of clean freshly voided urine on two separate occasions. The organisms are usually coliform bacilli, enterococci, or staphylococci.

The causes of dysuria and frequent urination in women without appreciable bacteriuria are uncertain. The symptoms have been ascribed to the "urethral syndrome," but this term has been criticised because there is no evidence of urethral disease in these patients² and it lacks a clear meaning. Many suggestions for an infective basis for these urinary symptoms have been proposed. Maskell³ proposed that urinary infection by "fastidious bacteria," such as *Lactobacillus*, *Streptococcus* spp and *Corynebacterium* spp might be responsible, but this has been denied by others.⁴ There is some evidence to suggest

that *Mycoplasma hominis* or *Ureaplasma urealyticum* infection may cause urinary symptoms.^{5,6} Dysuria may result from vulvovaginitis caused by *Candida albicans* or *Trichomonas vaginalis*.⁷ *Neisseria gonorrhoeae* infects the female urethra, and Curran⁸ found an association between urinary symptoms and the presence of this organism.

Recently, the role of *Chlamydia trachomatis* in the aetiology of urinary symptoms in women has been investigated. This organism can infect the female urethra, with or without concomitant infection of the cervix, and some women with urethral infections complain of dysuria.^{9,10} Stamm *et al*¹¹ studied 59 women with acute dysuria and frequent urination, without appreciable bacteriuria; patients with vulvovaginitis were excluded. They concluded: firstly that the two most common infectious agents associated with acute urinary symptoms in the women studied were *Escherichia coli* and *C. trachomatis*; secondly, that bacteriuria of $\geq 10^5$ organisms/ml may be an insensitive diagnostic criterion when applied to symptomatic lower urinary tract infection; and thirdly, that in this study *C. trachomatis* infection was implicated in most symptomatic women who had sterile bladder urine and pyuria. That important study firmly placed *C. trachomatis* infection among the possible causes of acute urinary symptoms in women.

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Sexually active women are subject to bacterial cystitis and are exposed to a wide variety of sexually transmitted organisms,^{12,13} and so care must be taken before attributing urinary symptoms to any one particular agent.^{14,15} In this study we have investigated possible correlations between lower urinary tract symptoms (dysuria and frequent urination), pyuria, and infection of the lower urogenital tract in a group of sexually active women.

Patients, materials, and methods

Two hundred and fifty six women were examined in the department of genitourinary medicine, University College Hospital, between January and September 1983. One hundred and thirty five (53%) attended because of symptoms, 85 (33%) because their sexual partners had sexually transmitted disease (STD), and 36 (14%) for a routine examination to exclude STD. Women who had taken antimicrobial drugs or used vaginal medication during the preceding two weeks were excluded; otherwise patients were unselected.

CLINICAL EXAMINATION

Patients in the study provided the following data during the initial interview: age; obstetric history; history of STD; history of urinary tract infection; reason for attendance at the clinic; symptoms; date of most recent sexual intercourse and number of sexual partners in the past month and the preceding six months; current contraception; and history of STD in recent sexual partners.

After the interview patients were examined in the lithotomy position. The vulva was cleaned with cotton wool. A cotton wool swab from vesicular or ulcerative lesions was taken for culture for herpes simplex virus, but viral culture from clinically normal epithelium was not attempted. A bivalve speculum was then inserted. The vaginal pH was tested with indicator paper. A drop of vaginal fluid was mixed on a slide with a drop of 10% potassium hydroxide solution and immediately smelled for a characteristic amine odour. Specimens were collected from the vagina for microscopy for clue cells, *T vaginalis*, yeast cells, and hyphae, and for culture for *Gardnerella vaginalis* and *C albicans*. The cervix was then wiped clean, and specimens were collected for microscopy and culture for *N gonorrhoeae* and for culture for *C trachomatis* and genital mycoplasmas. The speculum was then withdrawn; and specimens were collected from the urethra with a plastic loop for microscopy and culture for *N gonorrhoeae* and with endourethral wire cotton wool tipped swabs for culture for *C trachomatis* and mycoplasmas. A bimanual pelvic examination was then performed.

LABORATORY METHODS

N gonorrhoeae

Urethral and cervical specimens were Gram stained and examined for intracellular diplococci. Culture was on modified King's medium, with confirmation by coagglutination and sugar fermentation reactions.

C trachomatis

Culture was on McCoy cells pretreated with cycloheximide; inclusions were stained with iodine.

G vaginalis

Vaginal specimens were cultured on human blood agar.

M hominis and *U urealyticum*

Urethral swabs were placed in 1 ml of mycoplasma and ureaplasma phenol red broth; each was then diluted 10-fold into two further tubes of medium. These were incubated for 72 hours. Growth of *M hominis* and *U urealyticum* was identified by colour change and confirmed by subculture on solid medium. For the isolation of *M hominis* from urine an aliquot of 0.2 ml clean midstream urine was spread on to solid mycoplasma medium and incubated anaerobically for five days.

T vaginalis

Specimens suspended in 0.85% sodium chloride were examined at magnification x 400 for characteristic motile forms.

C albicans

A Gram stained vaginal smear was examined for yeast cells and pseudohyphae. Culture was on Sabouraud's medium.

Herpes simplex virus

Culture was performed on human embryonic lung cells.

Examination of urine

Midstream urine specimens were obtained and immediately sent to the laboratory where they were processed within four hours of collection. A 10 ml aliquot was centrifuged at 600 x g for 10 minutes and the deposit examined at magnification x 400. The number of polymorphonuclear leucocytes per mean of five fields was reported as 0, 1-5, 6-15, and >15. A 1 in 100 dilution of the urine was made in quarter strength Ringer's solution, and 0.1 ml aliquots of this and of the original urine specimen were spread on to cysteine lactose electrolyte deficient agar (Oxoid), which was incubated aerobically, and on to a blood agar plate, which was incubated anaerobically. Cultures were examined after 24 and 48 hours. All organisms present at a concentration of > 10² colony

forming units (cfu)/ml were identified using standard laboratory techniques. Table I shows the classification of pathogens into "accepted" and "doubtful".

TABLE I Classification of accepted and doubtful urinary pathogens

Accepted	Doubtful
<i>Escherichia coli</i>	Coryneforms
<i>Proteus mirabilis</i>	<i>Streptococcus milleri</i>
<i>Staphylococcus saprophyticus</i>	<i>Staphylococcus epidermidis</i>
<i>Streptococcus faecalis</i>	<i>Streptococcus</i> group G
<i>Klebsiella aerogenes</i>	<i>Streptococcus</i> group F
<i>Streptococcus</i> group B	<i>Streptococcus viridans</i>
<i>Staphylococcus aureus</i>	
<i>Bacteroides</i> spp	

Anaerobic vaginosis

The diagnostic criteria were: vaginal pH > 5.0, potassium hydroxide test positive, clue cells present, and no evidence of *T vaginalis* or *C albicans* on microscopy or culture.

STATISTICAL ANALYSIS

The data for each patient were coded and stored on the IBM (International Business Machines) 3081 computer at Cambridge University. Analysis was undertaken using SPSS (Statistical Package for the Social Sciences). Associations between variables were sought using the χ^2 test without Yates's correction; $p=0.01$ was chosen as the level of probability for significance. The degree of association between two variables (statistically unassociated at $p=0.01$) as was summarised using the ϕ coefficient, and the cross product ratio (odds ratio) with 95% confidence limits. The ϕ coefficient may be interpreted as a correlation coefficient with values close to zero indicating little if any association; values close to 1 indicate almost perfect association. Values of ϕ less than 0.30 are usually interpreted as indicating no more than trivial association. The odds ratio is equal to 1 for no association.

Results

PATIENTS

Age

The 256 women fell into the following age groups: <20 years ($n=12$, 5% of the total); 20-24 years ($n=95$, 37%); 25-29 years ($n=82$, 32%); 30-34 years ($n=32$, 13%); 35-39 years ($n=17$, 7%); 40-44 years ($n=6$, 2%); >45 years ($n=12$, 5%).

History of sexually transmitted disease

Of the 256 women, 14 (5%) gave a history of gonorrhoea and seven (3%) of infection by *C trachomatis*; 13 (5%) had been treated epide-

miologically as contacts of men with non-gonococcal urethritis (NGU), and 44 (17%) had had other infections such as genital warts, genital herpes, and trichomoniasis.

History of urinary tract infection

Fifty two (22%) had had one attack or urinary tract infection, five (2%) had had two attacks, and 17 (7%) three or more.

Symptoms

Fifty had urinary symptoms: 13 had frequency of urination without dysuria, 11 dysuria without frequency, and 26 had both frequency of urination and dysuria. There was an association between dysuria and frequency of urination ($p<0.001$). Only six women complained of urgent urination. Other symptoms included vaginal discharge in 74 (malodorous in five, odourless in 69), vulval irritation in 40, and vulval soreness in 28.

Sexual history

The patients were mostly sexually active; 139 (54%) had had intercourse during the week, and 186 (73%) during the two weeks, before attendance. Only eight (3%) denied intercourse during the preceding three months. The median time since the date of most recent intercourse was 7.1 days.

During the four weeks before attendance 190 (74%) women had had intercourse with only one partner, but 33 (13%) had had two partners, three had had three, and three had had at least four partners. Twenty six (10%) of the women had not engaged in sexual intercourse during this time. During the six months before attendance 153 (60%) of the women had had one partner, 56 (22%) had had two, 24 (9%) had had three, and 19 (7%) had had at least four; four of the women had not engaged in intercourse during this time.

Contraception

Contraception currently used by the women was: oral contraception in 128 (50%); intrauterine device in 30 (12%); diaphragm in 29 (11%); condom in 18 (7%); other methods in 13 (5%), and none in 38 (15%). Three of the women using no contraception were pregnant.

Sexually transmitted disease in recent partners

A history of sexual contact with a partner with STD during the four weeks before attendance was given by 111 (43%) of the 256 women as follows: partner with gonorrhoea (13), NGU (65), other STD such as genital warts, genital herpes, and pediculosis pubis (17), nature of infection unknown (16). Interestingly, though there was a history of contact with a partner with STD in 111 women, only 85 attended for this reason.

CLINICAL EXAMINATION

Examination of all the women showed the following: 15 (6%) had vulval condylomata acuminata; 51 (20%) showed vulval congestion and erythema (vulvitis); 20 (8%) had vulval ulceration; the urethral meatus was congested and oedematous in three. Fifty four (21%) showed vaginal congestion and erythema (vaginitis); 134 (52%) had a vaginal discharge that was considered to be abnormal by the examining physician, malodorous in 28, and odourless in 106. The cervix showed ectopy in 24 (9%) and congestion, oedema, and a mucopurulent discharge (cervicitis) in 51 (20%). Bimanual examination showed enlargement of the uterus in five women and adnexal tenderness in 14 (6%). There was suprapubic tenderness in six women and renal tenderness in three.

MICROBIOLOGY

Urethra

Polymorphonuclear leucocytes (PMNL) were present in Gram stained urethral smears as follows: <5 per x 1000 field, 216 (84%); 6-10 per field, 14 (6%); 11-15 per field, eight (3%); ≥ 16 per field, 18 (7%).

N gonorrhoeae was isolated from the urethra of eight (3%), *C trachomatis* from 21 (8%), and *M hominis* $> 10^2$ cfu/ml from 132 (52%) of the women. *U urealyticum* $> 10^2$ cfu/ml was recovered from 104 (81%) of the first 128 women; because of the high isolation rate this investigation was discontinued in the remainder.

Cervix

N gonorrhoeae was recovered from the cervix in 12 (5%), *C trachomatis* from 23 (9%), and *M hominis* $> 10^2$ cfu/ml from 99 (39%) of the women. *U urealyticum* $> 10^2$ cfu/ml was recovered from 67 (52%) of the first 128 women; this investigation was discontinued in the remainder.

Vulva

Herpes simplex virus was recovered from 11 (55%) of the 20 women with vulval ulceration. Because of the small numbers entailed, this organism was excluded from all analyses of association.

Vagina

The vaginal pH in the 256 women was between 3.0 and 7.0 (median 4.86). The potassium hydroxide test was positive in 79 (31%), clue cells were seen in 70 (27%), and *T vaginalis* was identified in 18 (7%) of the women. Vaginal culture yielded *G vaginalis* in 89 (35%) and *C albicans* in 72 (28%). Anaerobic vaginosis, as defined above, was present in 37 (15%) of the patients. *G vaginalis* was recovered from 27 of these 37 women.

Urine

The PMNL count in the MSU was 0/field in 172 (67%) of the women, 1-5/field in 57 (22%), 6-15/field in 14 (6%), ≥ 16 /field in seven (3%), and not reported in six (2%) of the 256 specimens. Accepted pathogens with a surface viable count $> 10^2$ /ml were recovered from 41 (16%) of 251 MSU specimens; the surface viable count was $\geq 10^5$ /ml in 24 of these 41 specimens. Doubtful pathogens were recovered from 20 (8%) of 250 MSU specimens; the surface viable count was $\geq 10^5$ /ml in five specimens. *M hominis* $> 10^2$ cfu/ml was recovered from 63 (26%) of 244 MSU specimens.

Multiple isolates

One organism was isolated from 78 (30%) of the 256 women, two from 55 (21%), three from 34 (13%), four from 27 (10%), and at least five from 16 (6%); the maximum number of separate isolates obtained from one patient was seven. Only 46 (18%) of the women yielded no isolates.

ASSOCIATIONS BETWEEN INFECTION OF DIFFERENT SITES

N gonorrhoeae was recovered from the cervix alone in four women, from the urethra alone in none, from both sites in eight, and from neither in 244 women. There was an association between the recovery of *N gonorrhoeae* from the urethra and cervix ($p < 0.001$). *C trachomatis* was recovered from the cervix alone in 10, from the urethra alone in eight, from both sites in 13, and from neither in 220 women. We did not have complete data on five women. There was an association between the recovery of *C trachomatis* from the urethra and cervix ($p < 0.001$).

M hominis $> 10^2$ cfu/ml was recovered from the urethra alone in 70 women, from the MSU alone in nine, from both sites in 54, and from neither in 109 women; results from the remaining 14 women were not available. There was an association between recovery of *M hominis* from the urethra and MSU ($p < 0.001$). An association was also found between the recovery of *M hominis* from the urethra and from the cervix ($p < 0.001$).

ASSOCIATION OF URINARY SYMPTOMS WITH EVIDENCE OF INFECTION

Frequency of urination

There was an association between frequency of urination and pyuria in the MSU ($p < 0.001$) (table II). There was a linear increase in the proportion of women with frequency as the PMNL count increased.

There was an association between frequency of urination and the isolation of undoubted pathogens from the MSU ($p < 0.01$) (table III). There was a linear increase in the proportion of women with frequency as the bacterial colony count increased. There was no

TABLE II Association between frequency of urination and pyuria

Frequency of urination	PMNL in centrifuged MSU/x 400 field:				
	0	1-5	6-15	>15	Total
Absent	155	44	10	3	212
Present	17	13	4	4	38
Total	172	57	14	7	250

PMNL = polymorphonuclear leucocytes.

MSU = midstream urine specimen.

Six patients did not have a PMNL count.

 $\chi^2 = 17.8$; $df=3$; $p<0.001$ linear trend in proportion with frequency:
 $\chi^2 = 16.9$; $df=1$; $p<0.001$.

association between frequency of urination and the isolation of doubtful pathogens.

No association was found between frequency of urination and the isolation of *C trachomatis* from either the urethra or the cervix, or from both sites (table IV). Likewise, there was no association between frequency of urination and the recovery of *M hominis* $> 10^2$ cfu/ml from the urethra, cervix, or MSU; the recovery of *N gonorrhoeae* from the urethra or cervix or both; recovery of *T vaginalis* or *C albicans* from the vagina; or the presence of bacterial vaginosis.

Dysuria

Associations were found between dysuria and pyuria ($p<0.002$) (table V); there was a linear increase in the proportion of women with dysuria as the PMNL count increased. There was also an association between dysuria and the isolation of undoubted pathogens from MSU ($p<0.001$) (table VI); there was a linear increase in the proportion of women with dysuria as the bacterial colony count increased. No associations were found between dysuria and the isolation of *C trachomatis* from the urethra, cervix, or either site (table VII), or the isolation of *M hominis* from the

TABLE III Association between frequency of urination and isolation of accepted pathogens from midstream urine (MSU) specimen

Frequency of urination	No of patients with log colony count/ml in MSU:			
	0	2-4	>5	Total
Absent	184	14	15	213
Present	26	3	9	38
Total	210	17	24	251

Five patients did not have culture for accepted pathogens.

 $(\chi^2 = 10.7$; $df=2$; $p<0.01$; linear trend in proportion with frequency:
 $\chi^2 = 9.71$; $df=1$; $p<0.01$).
TABLE IV Association of frequency of urination with recovery of *Chlamydia trachomatis* from urethra and cervix (χ^2 , ϕ coefficient, and odds ratio (95% confidence limits))

Frequency of urination	No of patients with <i>C trachomatis</i> isolated from:					
	Urethra			Cervix		
	Negative	Positive	Total	Negative	Positive	Total
Absent	200	16	216	196	18	214
Present	33	5	38	34	5	39
Total	233	21	254	230	23	253

Two and three patients did not have valid culture results from the urethra and cervix, respectively.

 $\chi^2 = 0.75$, $df=1$, NS
 $\phi = 0.074$
 $0 = 1.89$ (0.56, 6.02)

 $\chi^2 = 0.33$, $df=1$, NS
 $\phi = 0.055$
 $0 = 1.60$ (0.48, 5.00)

TABLE V Association between dysuria and pyuria

Dysuria	PMNL in centrifuged MSU/x 400 field				
	0	1-5	6-15	>15	Total
Absent	154	48	10	3	215
Present	18	9	4	4	35
Total	172	57	14	7	250

PMNL = polymorphonuclear leucocytes.

MSU = midstream urine specimen.

Six patients did not have MSU PMNL count.

 $(\chi^2 = 15.2$; $df=3$; $p<0.002$ linear trend in proportion with dysuria:
 $\chi^2 = 12.7$; $df=1$; $p<0.001$).

urethra, cervix, or MSU, or the isolation of *N gonorrhoeae*, *T vaginalis*, or *C albicans* from any site, or with the presence of bacterial vaginosis.

Frequency and dysuria

Similar associations were sought for the combination of these symptoms, but the patterns were the same as those found for either symptom alone.

TABLE VI Association between dysuria and isolation of accepted pathogens from midstream urine (MSU) specimen

Dysuria	No of patients with log colony count/ml in MSU			
	0	2-4	>5	Total
Absent	190	11	14	215
Present	20	6	10	36
Total	210	17	24	251

Five patients did not have MSU accepted pathogen count.

 $(\chi^2 = 24.6$; $df=2$; $p<0.001$; (linear trend in proportion with dysuria:
 $\chi^2 = 24.1$; $df=1$; $p<0.001$).

TABLE VII Association of dysuria with recovery of *Chlamydia trachomatis* from urethra and cervix (χ^2 , ϕ coefficient, and odds ratio (95% confidence limits))

Dysuria	No of patients with <i>C trachomatis</i> isolated from:					
	Urethra			Cervix		
	Negative	Positive	Total	Negative	Positive	Total
Absent	200	18	218	195	21	216
Present	33	3	36	35	2	37
Total	233	21	254	230	23	253

Two patients did not have valid culture results from the urethra and three from the cervix.

$$\chi^2 = 0.0; \text{df}=1; \text{NS} \quad \chi^2 = 0.29; \text{df}=1; \text{NS}$$

$$\phi = 0.001 \quad \phi = 0.053$$

$$O = 1.01 (0.34, 3.92) \quad O = 0.53 (0.08, 2.50)$$

ASSOCIATIONS OF URINARY SYMPTOMS WITH SPECIFIC PATHOGENS

Table VIII shows the rate of isolation of pathogens in women with and without urinary symptoms.

The only significant association found was that between urinary symptoms and accepted urinary pathogens. The odds ratios for the other organisms were reasonably close to unity, indicating lack of association with urinary symptoms. The 95% confidence limits of the odds ratio for some organisms, however, especially those with low prevalence such as

TABLE VIII Isolation of pathogens from women with and without urinary symptoms: percentage (denominator) and odds ratio (95% confidence limits)

Pathogen	No urinary symptoms	Urinary symptoms †	Odds ratio (95% CI)
<i>N gonorrhoeae</i>			
Urethra	3 (206)	4 (50)	1.39 (0.18, 7.96)
Cervix	4 (205)	6 (50)	1.39 (0.28, 5.91)
<i>C trachomatis</i>			
Urethra	8 (205)	10 (49)	1.34 (0.40, 4.19)
Cervix	9 (203)	10 (50)	1.14 (0.35, 3.50)
<i>M hominis</i> ($>10^2$)			
Urethra	55 (203)	42 (50)	0.60 (0.31, 1.17)
Cervix	41 (203)	32 (50)	0.68 (0.33, 1.38)
MSU	25 (197)	28 (47)	1.12 (0.52, 2.42)
<i>T vaginalis</i>	6 (206)	10 (50)	1.65 (0.48, 5.32)
<i>C albicans</i>	27 (206)	32 (50)	1.26 (0.61, 2.58)
<i>G vaginalis</i>	37 (202)	29 (48)	0.70 (0.33, 1.45)
Accepted urinary pathogen ($>10^3$)	7 (202)*	20 (49)*	3.44 (1.31, 9.02)
Doubtful urinary pathogen ($>10^3$)	2 (201)	0 (49)	0.36 (0.08, 4.84)

† Frequency of dysuria (includes six patients with urgency). Comparison of pathogens in two groups: * $p < 0.01$.

N gonorrhoeae, indicated that the odds on the presence of this organism in women with urinary symptoms could be as high as five or six times those in women without urinary symptoms.

ASSOCIATION OF URINARY SYMPTOMS AND TIME SINCE LAST INTERCOURSE

No associations were shown in this study between urinary symptoms and the number of days since the last sexual intercourse.

ASSOCIATIONS BETWEEN URETHRAL LEUCOCYTOSIS OR PYURIA AND SPECIFIC PATHOGENS

Urethral leucocytosis

Urethral leucocytosis, defined as the presence of >5 PMNL 1×900 field in a Gram stained urethral smear, was associated with the vaginal isolation of *T vaginalis* ($p < 0.001$) and *G vaginalis* ($p < 0.005$). It was not associated with the recovery of *C trachomatis*, *N gonorrhoeae*, *C albicans*, or urinary pathogens.

Pyuria

Table IX shows the relation between pyuria and the isolation of accepted pathogens from MSU. The two variables were associated ($p < 0.001$). There was no association between pyuria and the isolation of doubtful pathogens from MSU, the recovery of *C trachomatis* from the urethra, cervix, or either site (table X), or the recovery of *M hominis* from the urethra, cervix, or MSU. There was an association between pyuria and *T vaginalis* infection ($p < 0.005$) (table XI) but not with the recovery of *C albicans* or the presence of bacterial vaginosis.

Discussion

Over half of the unselected women whom we studied were symptomatic. The commonest symptom,

TABLE IX Association between pyuria and accepted pathogens in midstream urine (MSU) specimens

PMNL in centrifuged MSU	No of patients with log colony count/ml			
	0	2-4	5-6	Total
0	159	7	6	172
1-5	44	6	7	57
≥ 6	7	3	11	21
Total	210	16	24	250

PMNL = polymorphonuclear leucocytes.

Six patients without MSU counts of PMNL or accepted pathogens ($\chi^2 = 60.4$; $\text{df}=4$; $p < 0.001$).

With pyuria reclassified into absent (0 PMNL) and present (≥ 1 PMNL): $\chi^2 = 30.8$; $\text{df}=2$; $p < 0.001$; linear trend in proportion with pyuria: $\chi^2 = 30.7$; $\text{df}=1$; $p < 0.001$).

TABLE X Association between pyuria and *Chlamydia trachomatis* isolation from urethra and cervix (χ^2 , ϕ coefficient, and odds ratio (95% confidence limits))

Pyuria	No of patients with <i>C trachomatis</i> isolated from:					
	Urethra			Cervix		
	Negative	Positive	Total	Negative	Positive	Total
No	156	15	171	156	13	169
Yes	72	5	77	68	10	78
Total	228	20	248	224	23	247

Eight patients did not have midstream urine (MSU) specimen polymorphonuclear leucocytes (PMNL) count or urethra culture; nine did not have MSU PMNL count or cervical culture.

$$\begin{aligned}\chi^2 &= 0.13; \text{df}=1; \text{NS} & \chi^2 &= 1.11; \text{df}=1; \text{NS} \\ \phi &= 0.039 & \phi &= 0.082 \\ O &= 0.72 (0.22, 2.23) & O &= 1.77 (0.67, 4.6)\end{aligned}$$

described by 30% of the women, was vaginal discharge, but 20% complained of dysuria or frequency of urination or both; as these symptoms were statistically associated they may be considered together. These urinary symptoms are common among women seen in general practice and those who attend clinics providing services for young women, including STD clinics.^{12,16,17} Although structural and functional abnormalities of the bladder neck have been implicated, it is generally believed that in most cases these symptoms are due to infection, in particular acute cystitis, vulvovaginitis, and sexually transmitted infections. The patients examined in the present investigation were sexually active, and many of them gave a history of STD or urinary tract infection; they were therefore an appropriate group in which to study the aetiology of urinary symptoms in young women. As multiple infections were common in these women, a careful analysis was needed to determine associations between clinical and microbiological variables.

TABLE XI Association of pyuria with vaginal infection by *Trichomonas vaginalis*

<i>T vaginalis</i>	PMNL in centrifuged MSU			Total
	0	1-5	≥6	
Absent	164	53	16	233
Present	8	4	5	17
Total	172	57	21	250

PMNL = polymorphonuclear leucocytes.

MSU = midstream urine specimen.

Six patients did not have MSU PMNL count

($\chi^2 = 10.8$; $\text{df}=2$; $p<0.005$; linear trend in proportion with *T vaginalis*: $\chi^2 = 8.19$; $\text{df}=1$; $p<0.005$).

In seeking associations between variables, the χ^2 test has some disadvantages: it measures only the statistical significance of association and is dependent on the size of the sample. Generally, it is more useful to choose a statistic that measures the degree of association, such as the ϕ coefficient (an analogue of the correlation coefficient), or the odds ratio, for which 95% confidence limits may be readily calculated.¹⁸ These limits place bounds on the degree of association and thus aid interpretation of the χ^2 test, particularly when this is not significant at some chosen level of probability. In table VIII, for example, the limits on the odds ratio exclude an association between the presence of *G vaginalis* and urinary symptoms. It can also be seen, however, that the size of the sample does not exclude the possibility that the odds on *T vaginalis* in the presence of urinary symptoms could be over five times those in the absence of urinary symptoms. It should be noted, however, that the prevalence of this pathogen was low.

Dysuria or frequency of urination, or both, were strongly associated with the recovery of undoubted pathogens from the MSU; as the bacterial colony count rose the proportion of women with urinary symptoms also increased. A bacterial count of $\geq 10^5$ organisms/ml is the generally accepted criterion for separating a "significant" from an unimportant bacteriuria. Stamm *et al*¹⁹ suggested that a better diagnostic criterion for coliform infection of the lower urinary tract in symptomatic women would be $>10^2$ bacteria/ml. We agree that the level of bacteriuria regarded as "significant" may require redefinition, but before this can be done further studies of symptomatic and asymptomatic women with bacterial urinary tract infection in various clinical settings are needed.

In this study pyuria was associated with the isolation of accepted pathogens from the MSU, the level of pyuria increasing with the bacterial colony count (table IX); the definition of a level of pyuria that is important presents obvious difficulties, and in women with urinary infections its measurement does not seem to provide useful information for the clinician. Our results showed no association between doubtful pathogens and either urinary symptoms or pyuria.

Although vulvovaginitis was present in 20% of the patients, there was no association between urinary symptoms and the vulvovaginal pathogens *T vaginalis* and *C albicans*, or between urinary symptoms and bacterial vaginosis. Urethral leucocytosis and pyuria were both associated with *T vaginalis* infection. In other studies in this department (Yule, unpublished data) an association between trichomoniasis and urethral leucocytosis has been shown, and we were surprised that no association between trichomoniasis and urinary symptoms was shown in the present investigation.

Stamm *et al*¹¹ reported an association between

urogenital infection by *C trachomatis* and urinary symptoms. They studied 16 women with dysuria or frequency of urination, or both, who had pyuria but sterile bladder urine; seven of them yielded *C trachomatis* from the cervix or urethra, or both, and three others showed serological evidence of recent chlamydial infection: we were unable to confirm these results. *C trachomatis* was recovered from 31 of our patients, but an association between urethral or cervical infection, or both, by this organism and the presence of urinary symptoms could not be shown (table VII). Likewise, there was no association between dysuria or frequency of urination and the recovery of *N gonorrhoeae* from the urethra or cervix, or the isolation of *M hominis* from the urethra, cervix, or MSU. In our clinic population no associations between sexually transmitted infections and urinary symptoms could be shown.

Wallin *et al*²⁰ found a correlation between urethral leucocytosis (>10 PMNL/high power field) and infection by *C trachomatis* or *N gonorrhoeae*, but we were unable to show associations between these variables. Similarly, we found no association between pyuria and urethral or cervical infection by *C trachomatis* or both, although others have claimed to have done this.¹¹ Our results suggest that the symptoms and signs of urethral chlamydial infection are different in men and women. In men infection usually correlates with both urethral leucocytosis and pyuria,²¹ but our data indicated that, at least in our clinic population, these associations were not present in women. Suggestions that the "urethral syndrome" in women is analogous to non-gonococcal urethritis in men should therefore be considered cautiously, and it should be remembered that while dysuria is common in men with NGU, frequent urination is not. The pyuria in bladder urine, which Stamm *et al*¹¹ associated with chlamydial infection is unexplained, because *C trachomatis* is not known to infect vesical epithelium. The possibility that other pathogens may have a role in causing urinary symptoms in women with chlamydial infection has been raised.²²

How should a sexually active woman complaining of dysuria or frequency of urination, or both, be investigated? Our results show that culture of an MSU is essential but that both clinician and microbiologist should be willing to accept as significant a bacterial count below $>10^5$ organisms/ml, which is that which is usually recommended. The detection and measurement of pyuria seems to be less important. Culture for *C trachomatis* and *N gonorrhoeae* and microscopy for *T vaginalis* are investigations that should be performed in any sexually active woman, but not particularly because of urinary symptoms. Culture for *C albicans* and the diagnosis of bacterial vaginosis are important only for the elucidation of vulvovaginal symptoms. Culture for genital mycoplasmas does not

seem to us to be useful in the investigation of urinary symptoms. We found no association between these symptoms and the isolation of *M hominis* from the urethra or MSU, and *U urealyticum* was ubiquitous in our study group, having been recovered from the urethra of 80% of patients.

The aetiology of urinary symptoms in women is complex, and in the search for an explanation in women without urinary tract infection there is a growing tendency towards ascribing these symptoms to any pathogen found in the urogenital tract. Yet *C trachomatis*, *N gonorrhoeae*, *T vaginalis*, *C albicans*, and bacterial vaginosis can occur in women who not only have no urinary symptoms, but indeed, no symptoms of any kind. In future studies of urinary symptoms in women the role of non-infective causes, including autonomically mediated spasm of the smooth muscle sphincter²³ and psychological factors²⁴ may need to be reconsidered.

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